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Barriers to Adherence in Juvenile Idiopathic Arthritis: A Multicenter Collaborative Experience and Preliminary Results

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Abstract

Objective—Non-adherence is currently an under-recognized and potentially modifiable obstacle to care in juvenile idiopathic arthritis (JIA). The purpose of this study was to design and implement a standardized approach to identifying adherence barriers for youth with JIA across seven pediatric rheumatology clinics via the Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) and assess the frequency of adherence barriers in patients and their caregivers across treatment modalities.

Methods—An iterative process utilizing coproduction amongst parents and providers of patients with JIA was used to design the Barriers Assessment Tool (BAT) to screen for adherence barriers across four treatment modalities (i.e., oral medications, injectable medications, infusions, and

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physical/occupational therapy). This tool was implemented in seven rheumatology clinics across the United States and patient responses were collected for analysis.

Results—Data were collected from n=578 parents and n=99 patients (n=44 parent-child dyads). Seventy-seven percent (n=444) of caregivers and 70% (n=69) of patients reported at least one adherence barrier across all treatment components. The most commonly reported adherence barriers included worry about future consequences of therapy, pain, forgetting, side-effects, and embarrassment related to the therapy. There was no significant difference between endorsement of barriers between parents and adolescents.

Conclusion—Implementing a standardized tool assessing adherence barriers in the JIA population across multiple clinical settings is feasible. Systematic screening sheds light on the factors that make adherence difficult in JIA and identifies targets for future adherence interventions in clinical practice.

Key Indexing Terms

Juvenile Arthritis; Patient Compliance; Quality Improvement

Introduction

Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatic condition composed of seven unique phenotypic subtypes with varied clinical course severities and spectrums of morbidity.[1] The treatment landscape in JIA has rapidly evolved since the advent of biologic medications. Clinical trials focused on safety and efficacy have proven favorable prognostic outcomes when controlled dosing of medications are administered.[2–5] However, despite treatment advances, only 16-64% of the disease course is spent in a clinically inactive state when assessed across all JIA subtypes.[6] Even in patients who attain inactive disease status, the risk of flare within one year is 40%.[7] Moreover, long-term outcomes into adulthood reveal sustained limitations in functioning resulting in negative impacts on health-related quality of life.[8,9]

Non-adherence represents a modifiable factor that could significantly impact outcomes, including morbidity, mortality, costs, healthcare decision-making, and health-related quality of life.[10] Adherence is defined as the extent to which a person's behavior corresponds with provider health recommendations.[11] While adherence rates vary among general pediatric populations, average adherence is 50%.[12] Studies of adherence in JIA have been limited, with most focusing on self- and parent-reported adherence, which tend to be inflated relative to more objective measures (e.g., electronic monitoring). One study assessing adherence to non-steroidal anti-inflammatory medications in newly diagnosed JIA patients classified 52% of patients as adherent.[13] Interestingly, even more sophisticated therapies, such as biologic medications and disease modifying anti-rheumatic drugs (DMARDs), have suboptimal rates of adherence, with a mean medication refill possession ratio of 46.9% and 65.7% for subcutaneous methotrexate and injectable tumor necrosis factor- alpha inhibitors, respectively.[14] Factors predicting non-adherence in JIA include delayed time to therapeutic efficacy, fear of adverse effects, chronicity of disease and complex and costly regimens.[15–17] Conversely, factors associated with higher perceived adherence included perceived

helpfulness of treatment, lower disease severity and younger age of the child.[18] Despite what is known about non-adherence in JIA, there remains critical gaps in translating research findings into clinical practice. In fact, pediatric rheumatologists are unlikely to address adherence barriers in routine practice, especially when compared to treatment efficacy/performance.[16]

Identification of JIA-specific barriers is an important first step in adherence promotion, especially in clinical practice. The Health Belief Model postulates the importance of perceptions of barriers as a factor contributing to non-adherence, and served as a theoretical framework that prompted the systematic screening of barriers in our current study.[19] Research has demonstrated that as the number of patient-reported barriers increases, adherence to treatment decreases.[20] One study noted the impact of cumulative barriers, finding that each additional barrier to adherence increased the likelihood of non-adherence by approximately 30%.[21] Furthermore, we know from pediatric and adult literature that repeated measures of barriers to adherence are necessary as individual barriers are variable as the patient ages and disease status evolves.[22,23] Barriers identified in the larger pediatric literature (e.g., asthma, cystic fibrosis, solid organ transplant, inflammatory bowel disease) include forgetting, medication side effects or palatability, child oppositional behaviors and interference in daily life.[24–26] Understanding and identifying individual barriers will allow providers to target specific areas for intervention to promote adherence and self-management. Meta-analyses have demonstrated that multi-component interventions to address adherence can improve health outcomes and health care utilization.[27,28] Unfortunately, few studies have identified barriers to target for multi-modal adherence interventions in JIA, especially since the advent of biologic medications.

The current study used quality improvement methodology to design and test a barriers assessment tool specific for the JIA population, as well as to identify patient and parent-reported adherence barriers across several JIA treatments. The collaboration of a multi-center team of pediatric rheumatology providers, psychologists, and parent representatives was organized by the Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN). This international collaborative learning network is centered on the cooperative development and implementation of management strategies to improve the outcomes and quality care for patients with JIA. PR-COIN provided formal education and hands-on training in the field of self-management across seven of 18 PR-COIN member sites prior to the development of the adherence barriers screening tool. Our hypothesis was that this barrier assessment tool would comprehensively identify adherence barriers that would not have otherwise been discussed during a routine clinic visit. The second goal was to facilitate the systematic distribution of the barriers assessment across all seven sites. Finally, our team aimed to assess for concordance of adherence barriers across caregiver and patient dyad respondents. Consistent with prior literature, it was hypothesized that forgetting, side effects, and interference with daily life would be the most highly endorsed barriers across various treatment components (e.g., oral medications, injections, infusions, and physical and occupational therapy).

Patients and Methods

Design of the Barriers Assessment Tool

Seven centers (Children's Mercy Kansas City, Cincinnati Children's Hospital Medical Center, Cohen Children's Medical Center, Levine Children's Hospital, Stanford Children's Hospital, Nationwide Children's Hospital, and Penn State Children's Hospital) were involved in the design and implementation of the Barriers Assessment Tool through PR-COIN. A multidisciplinary co-production model was used, including pediatric rheumatologists, nurse practitioners, psychologists, and parents of children with JIA. Co-production is a collaborative approach in which all stakeholders including patients, caregivers and providers are involved in the project initiative from conceptualization to implementation. While this exact self-report measure was newly developed for this project, design of the Barriers Assessment Tool was based on prior work in other pediatric subspecialties.[24, 26,29,30] Validation studies have demonstrated that adherence barriers are strongly correlated with both adherence and health outcomes (e.g., organ rejection, seizures).[26,29,30] An iterative process via monthly teleconferencing was utilized to create, modify, and individually tailor the Barriers Assessment Tool for patients with JIA. Engagement of the families in the feedback and design process was valuable in tailoring a tool that would be specific to this unique population. Important re-design feedback included reconfiguring the tool to ease usability, as well as altering the checklist to include JIA-specific barriers across various treatment components. Streamlined design was of paramount importance to the co-production team with emphasis on keeping the tool limited to one page in length. Care was taken to limit word density and check-boxes were utilized to further simplify the tool. An important goal of the team was to avoid contributing to "form fatigue" and provide the most information with the least amount of patient or caregiver effort. The final Barriers Assessment Tool is composed of a 17-item checklist spanning four treatment modalities-oral medications, injections, infusions and physical/occupational therapy. Barrier themes include regimen characteristics (i.e. palatability and complexity), logistical impedances, patient oppositional behavior, social difficulties and efficacy concerns. Although the general layout remained consistent between the tools designed for other patient populations (e.g., kidney transplantation and epilepsy), specific barriers and treatment regimens were added. Examples of JIA specific regimens included the addition of injections, infusions and physical/occupational therapy. Worry for future side effects and concern for future child-bearing were barriers that patients and caregivers independently identified in JIA, in addition to more universal barriers (i.e. forgetting or poor taste). Two versions of the assessment were designed, one for caregivers and one for children 10 years old or older. Age 10 was chosen based on developmental ability to independently complete the forms.

Implementation of the Barriers Assessment Tool

The Barriers Assessment Tool was successfully administered to patients and/or parents at the seven PR-COIN centers. Cincinnati Children's Hospital Medical Center (CCHMC) served as the Central IRB and the coordinating center for the study. The study protocol was first approved through the Central IRB (IRB #2010-2811). Additionally, local IRB approval of the protocol was obtained for the following sites: Cohen Children's Medical Center, Levine Children's Hospital, Stanford Children's Hospital, Nationwide Children's Hospital, and

Penn State Children's Hospital. All scheduled patients with JIA during the seven-month testing period (March – September 2016) were eligible to participate. Participants represented all JIA subtypes and ages and had to be currently receiving one or more of the treatment modalities (oral medications, injections, infusions or physical/occupational therapy) at the time of participation. Informed consent was not required by respective institutions as this was undertaken as a quality improvement initiative. All parents were asked to complete a Barriers Assessment Tool, and children 10 years old or older were given their own form to capture parent-patient dyad responses. Improvement science principles and tools were applied across sites to facilitate the work, including development of a Key Driver Diagram, process flow maps, iterative Plan-Do-Study-Act (PDSA) cycles based upon key drivers to design reliable implementation processes. The Model for Improvement was utilized as the framework to guide the process and improve integration into care delivery.[31] The primary process measure was the percent of indicated Barriers Assessment Tools that were successfully collected. As this was a quality improvement initiative, patient identifiers were not linked to completed questionnaires and thus demographics (i.e. JIA subtype, age, race, disease severity) were unable to be obtained in the current project.

Teleconferencing was used to share data and the experience of implementation in varying busy clinic flow scenarios. The group problem-solved ways to improve execution. Site-specific processes of implementation varied based on local staffing resources; however, broad solutions included clearly defining staff responsibilities and linking distribution of the assessment to an already established process, such as morning clinic set-up. Although there was no measurement of the visit time burden of introducing this tool, there was provider feedback that the tool allowed a swift inventory of patient or parent concerns that led to productive conversations. While repeat measurements from the same patient were possible, this was unlikely given the short testing time-frame in relation to typical JIA follow up appointment timing.

Statistical Analysis of Barriers Assessment Tool Responses

Descriptive statistics, including means, standard deviations, and frequencies, were used to examine barriers. Each barrier was scored as either '0' (not endorsed) or '1' (endorsed). We used paired-sample *t* tests to assess frequency differences in barriers across treatment modalities. McNemar tests were conducted to examine differences in the endorsement and concordance between parent-child dyads. Analyses were performed with the Statistical Package for Social Sciences (SPSS), Version 24.[32]

Results

Endorsement and Types of Barriers

A total of 677 barrier assessments were collected out of 1148 eligible patients over the study testing period (59% completion rate). The collected assessments included 578 parent and 99 patient responses, with 44 identified parent-child dyads across the seven participating PR-COIN sites. Of those respondents, 76.8% (n=444) parents and 69.7% (n=69) patients reported at least one adherence barrier across all treatment components. The most commonly endorsed barriers among patients and parents stratified by treatment modality are presented

in Figure 1 and 2. Notably, worry about future treatment consequences, pain, forgetting, side effects, and embarrassment were the top barriers among both parents and patients.

Barriers to oral medications were endorsed in 44.6% (n=258) of parents and 47.5% (n=47) of patients. Top oral medication barriers included worry about future consequences, forgetting and poor taste. Barriers of any type for injectable medications were endorsed in 52.5% (n=304) of parents and 40.4% (n=40) of patients. Infusion barriers were endorsed in 12.7% (n=73) and 9% (n=9) of parents and patients respectively. The most highly endorsed barriers for both injectable and infusion medication were worry, pain and side effects. Barriers to physical and occupational therapy were noted in 13% (n=75) of parents and 14% (n=14) of patients. The top reported barriers for physical and occupational therapy were forgetting, pain and believing the therapy is unnecessary.

Most parents (M=2.83± 3.20) and patients (M=2.80± 2.90) endorsed less than three barriers. The number of injection barriers endorsed (M=1.37+1.73) was significantly higher compared to oral medications (M=0.95+1.43; p <0.01) in parents. No significant differences were found among treatment modalities for the frequency of patient-reported barriers.

Caregiver-Patient Convergence on Barriers to Adherence

McNemar tests were performed to examine differences in the endorsement of barriers between the forty-four parent-patient dyads. Separate tests evaluated for agreement for each barrier per treatment modality. Both parents and patients tended to agree on barriers endorsed within categories of therapy. No significant differences were found between the barriers endorsed for oral medications (16% vs. 19%), injections (24% vs. 22%), infusions (3% vs. 4%), or physical/occupational therapy (10% vs. 11%) between the dyads.

Discussion

The current study sought to systematically assess parent and patient treatment barriers in JIA across individual treatment modalities through the leverage of a learning network. The majority of participants expressed at least one barrier to a treatment modality, which highlights the importance of such a screening tool to encourage discussion of treatment adherence in clinical care. This is a new addition to our current care framework which does not currently emphasize screening for adherence barriers as compared to addressing therapeutic performance.[16]

Common barriers endorsed included largely actionable concerns, such as poor taste, forgetting, pain and difficulty managing side effects. Evidence-based treatments to address several of these barriers have been developed and have been found to be efficacious.[33–35] The provision of intervention tools to address these common barriers with patients and caregivers in clinical practice is critical to addressing the needs of the patient and improving adherence. A pilot adherence initiative in kidney transplantation has found that systematically identifying and addressing adherence barriers to immunosuppressant therapy improved population-based outcomes (i.e., late organ rejection).[36]

The most commonly endorsed barrier across all treatment modalities was worry about future consequences of receiving the therapy. This is a JIA-specific barrier that has not been identified in other pediatric populations but is quite salient with the use of biologics, which have relatively short term data regarding adverse effect risks in children.[37,38] Familial assurance regarding appropriate therapeutic decisions balanced against the risk of long term disease-related damage is largely up to individual providers, making this a variable experience overall.[39] One qualitative study of pediatric patients prescribed tumor necrosis factor- alpha inhibitor biologics highlighted that the current education and decision making process in rheumatology and gastroenterology clinics ultimately led to long-term worry and concern surrounding therapy.[40] Families acquire information about prospective therapies from multiple sources, including medical care providers, the internet and social contacts, making clear access to unbiased and timely information more important than ever.[41] Shared-decision making techniques could be beneficial in reducing concern and uncertainty and ultimately improve adherence to treatment recommendations. Systematically implementing patient-centered tools or decision aides for treatment education is one way to navigate varying patient and provider approaches.[42]

Interestingly, injectable medications, which are most often given in the home by either the patient or parent, had the highest endorsement of barriers, even when compared to hospital infusion therapy. These findings suggest that home-based injections may create a more burdensome experience for families when compared to hospital infusions. This may be counterintuitive because hospital infusions require additional transportation and time requirement for families. While common injection barriers include pain, discomfort and refusal, worry about future consequences was also markedly higher in families receiving injectable medications compared to infusion therapy. It is possible that the actual act of caregivers or patients administering injections, rather than hospital staff, amplifies these concerns despite the added convenience that an in-home injection could provide. While this is the first time a comparison of perceived worry between injectable and infusion therapy has been attempted, the impact of the general care of patients with JIA on psychological health and quality of life for caregivers has been established in our population.[43] This finding could suggest that increased training initiatives and education surrounding injection administration may be helpful to prevent such barriers.

Although no differences were found between parents and patients in either number or type of barriers expressed, we still believe it is important to gather both perspectives. It has been previously described that adolescents with JIA and their parents exhibit meaningful differences in their responses regarding treatment helpfulness and adherence.[44,45] Formal screening and discussion of potential discrepancies may help to facilitate communication between provider, patient and caregiver to better understand differing goals of therapy. While there is variability in age at which adolescents transition to assuming more responsibility of their medication and exercise regimens, this is an important time of skill building for fostering interest in their own care. In a study involving initiation of biologic therapy in JIA and Crohn’s Disease, most adolescents valued the involvement of their physician or parent in treatment decisions, but given the chance would have preferred more active participation and dedicated education.[46]

There are some notable limitations to this study that deserve consideration. While our barriers assessment tool was newly designed for this project without formal validation, the themes depicted in our tool have been systematically and rigorously validated in other pediatric chronic illness populations.[26,29,30] A correlation of our tool with quantitative measurement of adherence would have been optimal to translate endorsed barriers with actual behavior. Self- or parental-reported adherence would have also added to the richness of this data. Additionally, participant demographics were not collected in keeping with restrictions of a multi-center quality improvement project design; thus, we were unable to examine differences in barriers by patient age, disease duration, disease severity and treatment regimen complexity. Moreover, while our sample size was large, there were a small number of parent-patient dyads to assess for comparisons. Regardless, the multicenter design and unique coproduction model that was utilized for this study make it novel and innovative in the field of JIA adherence research.

By harnessing the collective coordination of a learning network, PR-COIN was able to lead the design and implementation effort of this Barriers Assessment Tool as part of a large, multi-center self-management initiative. Tracking introduction of the tool across sites allowed us to ensure feasibility in delivery of the tool across seven clinical settings. Both parent and provider feedback of the tool's usability during both the design and delivery of the tool was encouraging that it can be successfully used to screen for and facilitate discussions surrounding non-adherence in any pediatric rheumatology clinic. Since its development, the BAT has been distributed for use among all 18 PR-COIN sites as part of a larger self-management optimization package. For access to this tool for research or clinical purposes, please contact the authors.

Future directions of this work will include design and testing of complementary adherence promotion tools to contribute to a larger systems-level adherence initiative. For example, multiple solutions to improve taste or forgetting medications have been used to improve adherence.[47,48] Using such tools to increase dialogue between pediatric rheumatology providers and patients/families to identify and test various solutions based on individual needs (e.g., text-messages to remind people to take medications if they like technology or pairing medications with routines like brushing teeth) could be beneficial. Further, use of a standard set of adherence tools by clinical providers would systematize adherence solutions across patients. As with other chronic pediatric illnesses, formalizing adherence screening as a part of clinical care in JIA would likely continue to improve outcomes of this population. In JIA specifically, patient perceived adherence was related to better health related quality of life, particularly with gross motor and psychosocial functioning.[44] Better adherence has also been linked to improvements in short-term outcomes in JIA including lower joint counts, improved physical functioning scores and parental perception of global improvement.[49] These findings continue to support the investigation and clinical emphasis in addressing adherence barriers in JIA. It is our intention to facilitate and ease discussions surrounding adherence behaviors and provide a usable system that will translate to more effective care in the JIA population.

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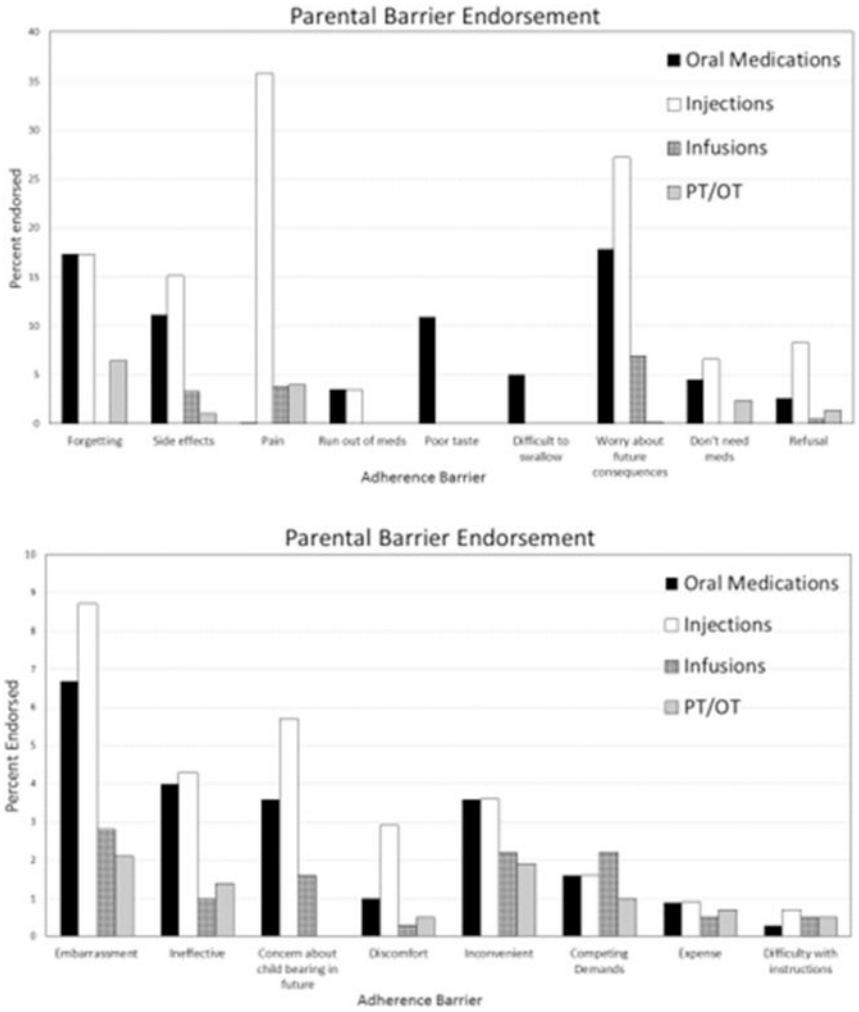

Figure 1.

a and b Frequency of Parental Endorsed Barriers across Treatment Modalities.

This bar graph indicates the percentages of adherence barriers endorsed on the barriers assessment tool among parental respondents.

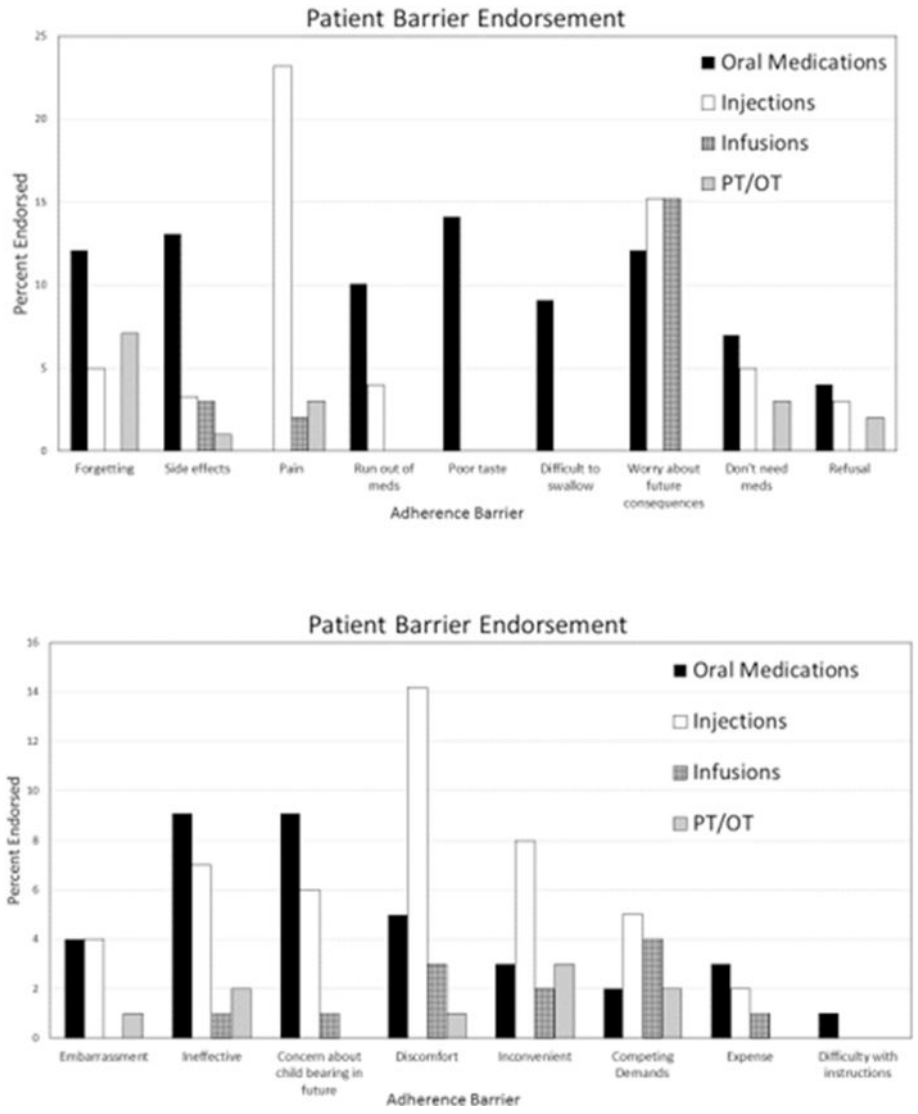

Figure 2.

a and b Frequency of Patient Endorsed Barriers across Treatment Modalities.

This bar graph indicates the percentages of adherence barriers endorsed on the barriers assessment tool among patient respondents.